

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
13 October 2005 (13.10.2005)

PCT

(10) International Publication Number
WO 2005/094822 A1

(51) International Patent Classification⁷: A61K 31/4406,
31/44, C07D 213/16, 213/18, 213/85, 213/89, 213/61,
213/65, A61P 25/28, 29/00

(21) International Application Number:
PCT/US2005/007507

(22) International Filing Date: 9 March 2005 (09.03.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/555,137 22 March 2004 (22.03.2004) US

(71) Applicant (for all designated States except US): ELI
LILLY AND COMPANY [US/US]; Lilly Corporate
Center, Indianapolis, IN 46285 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): AGEJAS-
CHICHARRO, Francisco, Javier [ES/ES]; Lilly, S.
A., Avenida de la Industria 30, E-28108 Alcobendas,
Madrid (ES). DRESSMAN, Bruce, Anthony [US/US];
1430 North New Jersey, Indianapolis, IN 46202 (US).
GUTIERREZ SANFELICIANO, Sonia [ES/ES]; Lilly,
S. A., Avenida de la Industria 30, E-28108 Alcobendas,
Madrid (ES). HENRY, Steven, Scott [US/US]; 3362 South
Southway Drive, New Palestine, IN 46163 (US). MAR-
TINEZ PEREZ, Jose, Antonio [ES/ES]; Lilly, S. A.,
Avenida de la Industria 30, E-28108 Alcobendas, Madrid
(ES). MASSEY, Steven, Marc [US/US]; 3525 Waterstone
Court, Indianapolis, IN 46268 (US). MONN, James,
Allen [US/US]; 7518 Allenwood Court, Indianapolis, IN
46268 (US). ZIA-EBRAHIMI, Mohammad, Sadegh
[US/US]; 7724 Cove Court, Indianapolis, IN 46254 (US).

(74) Agents: ANDERSON, Arvie, J. et al.; ELI LILLY AND
COMPANY, P. O. Box 6288, Indianapolis, IN 46206-6288
(US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
ZM, ZW.

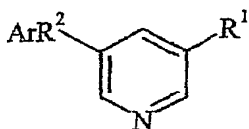
(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted
a patent (Rule 4.17(ii)) for the following designations AE,
AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,
EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA,
ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ,
NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT,
BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK,
TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG)

[Continued on next page]

(54) Title: PYRIDYL DERIVATIVES AND THEIR USE AS MGLU5 RECEPTOR ANTAGONISTS



(1)

(57) Abstract: The present invention is directed toward pyridyl derivatives of formula (I) as antagonists of the mGlu5 receptor. As such the compounds may be useful for treatment or prevention of disorders remedied by antagonism of the mGlu5 receptor, wherein Ar is phenyl or naphthyl each of which may be substituted by one or more C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₅ acyl, halo, amino, nitro, cyano, hydroxy, C₁-C₅ acylamino, C₁-C₄ alkylsulfonylamino, mono-, di- or trifluorinated C₁-C₃ alkyl, substituents which may be the same or different and may bear a CONH₂, CONHCH₃, CON(CH₃)₂, CO₂H, CO₂CH₃, OCF₃, CH₂NHCOCH₃, CH₂NH₂, CH₂N(CH₃)₂, CH₂CN, CH₂OH, CH₂NHSO₂CH₃, CH₂N(CH₃)(CH₂)₂ CN, CH₂N(CH₃)CH(CH₃)₂, CH₂NHCH(CH₃)₂, CH₂NH(CH₂)₂CH₃, CH₂NHCO₂R⁴, CH₂NHCH₂CH₃, CH₂NHCH₃ NHCOC(CH₃)₂, or N(S(O)₂CH₃)₂

substituent; R¹ is hydrogen, halo, R⁴, CN, C(NO⁺H)R³, C(NO⁺-R⁴)R³, (CH₂)₂CO₂R⁴, (CH₂)_n OR³, COR³, CF₃, SR⁴, S(O)R⁴, S(O)₂R⁴, COCH₂CO₂R³, NHSO₂R⁴, NHCOR³, C(NOR³)NH₂, CH₂OCOR³, (CH₂)_n NH₂, CON(CH₃)₂ (CH₂)_nNHCO₂R⁴, CO₂R³, CONH₂, CSNH₂, C(NH)NHOR³, (CH₂)_nN(CH₃)₂, or CONHNHCOR³; R² is 1,2-ethenediyl or 1,2-ethynediyl; R³ is hydrogen or C₁-C₄ alkyl; R⁴ is C₁-C₄ alkyl; and n is 0, 1, 2, 3 or 4; or a pharmaceutically acceptable salt thereof, or an N-oxide thereof.



- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT,

BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

- of inventorship (Rule 4.17(iv)) for US only

Published:

- with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.